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N80-21974

Unclas
46857

NASA TM-76012

G.A. Makarov

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON D.C. 20546 JANUARY 1980

JANUARY 1980



UDC 612.766.2-08:612.173.1.015.348.014.464:612.274

EFFECT OF HYPERBARIC OXYGENATION IN CARBOHYDRATE
METABOLISM AND PROTEIN SYNTHESIS IN THE MYOCARDIUM
DURING SUSTAINED HYPODYNAMIA

By

G. A. Makarov*

Prolonged restricted motor activity (hypodynamia) is one of the factors that detrains the cardiovascular system and the apparatus of its regulation, and promotes the appearance of atherosclerosis, coronary insufficiency, disorders in the contractile capacity of the myocardium, and orthostatic instability all the way to collapse [2, 4]. The most significant changes during hypodynamia are characterized by a disorder in the water-salt exchange [9], weakening of hormonal activity and exhaustion of the supplies of catecholamines in the tissues [10], decrease in the synthesis of tissue proteins and increase in the breakdown [16], and change in the processes of energy formation in the myocardium [6, 13]. The severe conditions of prolonged hypodynamia are characteristic for the clinical treatment of cardiovascular diseases, in particular, myocardial infarct. Here often unfavorable changes are observed in the metabolic processes aggravating the course of the main disease, and rehabilitation of such patients to a considerable measure depends on the elimination of the consequences of the forced hypodynamia.

Recently in the treatment of many cardiovascular diseases occurring with distortion of myocardial metabolism, hyperbaric oxygen treatment has been successfully used [14, 20]. Taking into consideration the increase in the energy potential of the tissues and the favorable reconstruction of different metabolic links

*Department of Pathological Physiology of I. P. Pavlov Ryazan' Medical Institute.

**Numbers in margin indicate pagination in original foreign text.

during the effect on the organism of slight pressure of pure oxygen [5,7] it seemed expedient to us to study the effect of hyperbaric oxygenation on the main processes of vital activity of the myocardium--bioenergetics and plastic supply of the functions, effectiveness and lability of which determine as a result the adaptation of the organism to the various extreme situations [8], including prolonged hypodynamia.

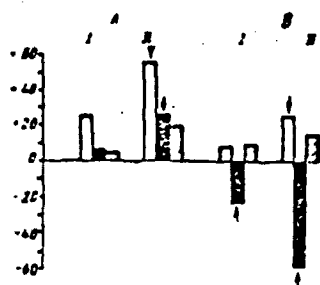
Material and Methods

Experiments were conducted on 140 albino male rats weighing 170-240 g. Hypodynamia was created by keeping the animals for 45 days in close individual cages that restrict the mobility of the animals in all directions. In the last 2 days the animals were placed for 3 h in a decompression chamber with pure oxygen under pressure of 1.5 ata, i.e., under conditions of hypoxia that did not have a toxic effect on the organism [1, 7]. The oxygen was periodically exchanged; carbon dioxide and water vapors in the chamber (volume 15 l) were absorbed by soda lime and silica gel. After exposure in the decompression chamber the rats were kept for 3 h under normal conditions, then they were killed; the effect of oxygen on the metabolic processes even after a single session for 1 h was preserved for over 24 h [5]. Analogously hyperbaric oxygenation was conducted on intact animals. The intensity of glycolysis in the system of energy production of the myocardium was judged from the change in the content of substrates: glycogen [12], pyruvate [18], lactate [17], lactate/pyruvate coefficient and activity of enzymes of glycolysis: aldolase [15] and lactate dehydrogenase--LDH [21]. The activity of aldolase was expressed in conventional units of LDH--in the blood in Vroblevskiy units, in the myocardium--in micromoles per minute for 1 g. The intensity of protein synthesis in the mitochondria and post-mitochondrial supernatant was judged according to the rate of inclusion of glycine- C^{14} introduced intraperitoneally in a dose of 25 μ Cu per 100 g of weight 6 h before death. The mitochondria were isolated by the method of differential centrifuging [11] in 0.25 M solution of sucrose (pH 7.4) with 0.001 M of EDTA. The protein of the mitochondria and supernatant was precipitated by a 10% solution of trichloroacetic acid, reprecipitated by a 5% solution of it, then successively washed with alcohol, mixture of alcohol and ether (1:1), ether and dried for 12 h at 60°. The radioactivity of the preparations was measured on an end-type counter BFL-T-25 with conversion unit PP-16. The specific activity was expressed in impulses per minute for 10 mg of protein.

Results and Their Discussion

Prolonged hypodynamia induced in the animals serious changes in the metabolism of the myocardium resulting in reconstruction of the processes of energy formation and decrease in the plastic supply of the functions. Thus, in the myocardium the amount of pyruvic (by 17.6%) and lactic acids (by 53.6%) increased, the lactate/pyruvate coefficient increased; its rise reflects the hypoxic nature of metabolism in the tissues [19]. A considerable exhaustion of the supplies of glycogen was also noted (by 56.7%). The increase in the lactate/pyruvate coefficient observed during hypodynamia, as well as a significant increase in the activity of the enzymes of glycolysis (see figure)--aldolase (by 56%), and LDH (by 25.5%)-- indicate the significant intensification of the processes of glycolysis and glycogenolysis, inhibition of pyruvate inclusion in the Krebs cycle and shift in the lactate dehydrogenase reaction towards the accumulation of lactic acid.

Analogous changes in the content of substrates and activity of the enzymes of glycolysis were also observed in the blood of animals with hypodynamia (see table and figure).



Change in Activity of Aldolase and Lactate Dehydrogenase (in % of changes of control) during Hypodynamia and Effect of Hyperbaric Oxygenation

A--aldolase; B--lactate dehydrogenase; I--blood; II--heart. Light columns--hypodynamia, dark--hyperbaric oxygenation, hatched--hypodynamia and hyperbaric oxygenation. Arrows indicate statistically reliable differences with the control. ($p < 0.5$)

Intensification in the power of glycolysis in the myocardium of the experimental animals, apparently, is a compensatory factor in maintaining the energy potential, for during hypodynamia there is a considerable reduction in oxygen consumption by the homogenates of the heart with the use of various substrates [3], as well as a drastic inhibition of the processes of oxidative phosphorylation [13] i.e., the effective functioning of the mitochondria, the main power generators of the cell, is blocked. In an electron microscopic study in these same periods of hypodynamia swelling of the mitochondria, reduction in them of the quantity

cristae, disorder in the structure of the cellular membranes were revealed [3,4], i.e., changes that indicate a deficit of oxygen.

CHANGE IN INDICES OF CARBOHYDRATE METABOLISM AND PROTEIN SYNTHESIS IN RAT MYO - CARDIUM DURING PROLONGED HYPODYNAMIA AND EFFECT OF HYPERBARIC OXYGENATION

Series of experiment	Statistical indicator	Gly-cogen	Pyruvate mg%		Lactate		Lactate/pyruvate coefficient		Inclusion of glycine-C ¹⁴ in protein (in imp/min per 10 mg of protein	
			blood	myo-cardium	blood	myo-cardium	blood	myocar-dium	mito-chondria	super-natant
Control (Intact animals)	M	430	2.0	1.7	15.8	13.8	7.9	8.1	360	308
	$\pm m$	20.0	0.12	0.09	1.2	0.9			21.6	25.8
	n	8	6	6	6	6	6	6	6	6
Hypodynamia	M	186*	1.9	2.0*	20.9*	21.2*	11.0	10.6	188*	164*
	$\pm m$	8.5	0.07	0.1	1.3	1.4			16.4	11.6
	n	10	8	8	8	8	8	8	6	6
Hyperbaric oxygenation	M	402	2.96*	2.14*	13.6	12.3	4.6	5.7	498*	390*
	$\pm m$	19.2	0.13	0.16	1.12	1.1			26.6	19.9
	n	8	6	6	6	6	6	6	6	6
Hypodynamia and hypertaric oxygenation	M	348*	2.0	1.9	18.0	16.9*	9.0	8.9	322	230*
	$\pm m$	19.9	0.12	0.08	1.0	1.0			15.3	10.5
	n	7	8	8	8	8	8	8	6	6

Designations: *--differences with control are statistically reliable ($p < 0.05$); n--number of experiments.

Naturally, under these conditions the plastic supply of the myocardial functions is also reduced. In the experimental animals a sharp inhibition was noted of the incorporation of glycine-C¹⁴ (see table) in the total protein of the mitochondria (by 53.3%) and supernatant (by 56.9%). Apparently, the reduction in the level of phosphorylation in the myocardium leading to a delay in the process of formation of macro-ergic phosphorous compounds, and depression of the reparative processes are the basis for the observed detraining of the heart during hypodynamia and drop in its weight [2].

Taking into consideration the favorable changes in metabolism and intensification in the energy potential of the tissues in hyperbaric oxygenation [1, 7] we considered it expedient to use this biological method of intensifying the adaptation reserves of the organism during hypodynamia.

Exposure of intact animals in a medium of pure oxygen induced in the blood and tissues of the heart a considerable reduction in the lactate/pyruvate ratio and decrease in the activity of LDH (see figure), which indicates the dominance of the oxidative transformations of the substrates in the Krebs cycle [19]. The observed increase in activity of aldolase and concentration of pyruvate on the background of a reduction in the content of lactate indicates the intensification

of the functioning of the Embden-Meyerhof cycle, here the resynthesis of glycogen remains on the optimal level. In a study of synthetic processes in the subcellular fractions of the myocardium an increase was revealed in the intensity of protein synthesis in the mitochondria by 38.3%, in the supernatant by 27.4% (see table).

Hyperbaric oxygenation had a favorable metabolic effect on the animals with hypodynamia. In the blood and myocardium a reduction was noted in the quantity of lactic and pyruvic acids, the lactate/pyruvate ratio, and glycogen synthesis increased in the myocardium. The activity of aldolase and LDH was almost normalized (see figure). Light hyperbaric oxygenation, increasing the consumption of oxygen by the homogenates of the heart and the effectiveness of oxidative phosphorylation in the intact animals [1,5] probably governs, judging from our data, the similar changes in the myocardium of rats during hypodynamia, which creates the necessary energy base for intensification of the reparative processes. In fact, the intensity of protein synthesis in the cytostructures of the myocardium, especially in the mitochondria, in rats of this series was considerably more pronounced than in animals with hypodynamia, and approached the normal.

Thus, taking into consideration the favorable effect of light hyperbaric oxygenation on the metabolic processes in the myocardium, it is expedient to include hyperbaric oxygen therapy in the arsenal of resources for directed effect on the myocardial metabolism in the case of forced prolonged hypodynamia. The unidirectional nature of changes in the activity of glycolytic enzymes, concentration of substrates and lactate/pyruvate ratio in the blood and myocardium in experimental animals and in the period of hyperbaric oxygenation makes it possible to use these hematological indices as criteria for evaluating metabolic shifts in the myocardium.

Conclusions

1. Prolonged restricted motor activity in animals induces in the blood and myocardium an increase in the concentration of lactic and pyruvic acids, lactate/pyruvate coefficient, activity of glycolytic enzymes--aldolase and lactate dehydrogenase, exhaustion of supplies of glycogen and reduction in intensity of protein synthesis in subcellular fractions of the myocardium.

2. Hyperbaric oxygenation, increasing the oxidation of pyruvate

and intensity of synthetic processes in the myocardium, leads to a reduction in the concentration of pyruvate and lactate in the blood and myocardium of animals with hypodynamia; here the activity of the enzymes of glycolysis is normalized and the intensity of the reparative processes in the myocardium is considerably increased.

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